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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,660	08/22/2000	Jonathan Schneck	01107.00042	9271

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	16

DATE MAILED: 06/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/642,660	SCHNECK ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-32 and 51-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32 and 51-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/8/2003 has been entered.

2. Claims 28-32 and 51-60 are pending and examined on the merits.

Claim Rejections Withdrawn - 35 USC § 112, 2nd paragraph

3. The rejection of claims 56 and 57 under 35 USC 112, 2nd paragraph is withdrawn in view of the amendments filed by the applicant.

Claim Rejections Withdrawn - 35 USC § 112, 1st paragraph

4. The rejection of claims 28-32 and 51-60 under 35 USC 112, 1st paragraph for lacking an enabling disclosure is withdrawn.

Claim Rejections - 35 USC § 112, 2nd paragraph

5. Claims 28-32 and 51-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. With regard to claims 28 and dependent claims thereof, it is unclear as to how the extracellular domain of the transmembrane polypeptide forms the binding domains when the said polypeptide is linked or conjugated to the variable domains of an

immunoglobulin. Does steric hinderance from the variable domains of an immunoglobulin interfere with the binding of ligands to the extracellular domain of the transmembrane protein?

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 28-32 and 51-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,015,884 in view of Seimiya H *et al* (J Biochem (Tokyo) 1993 Jun;113(6):687-91). Claims are drawn to a composition comprising a cell that comprises at least four fusion proteins, wherein the fusion proteins comprise either an Ig heavy chains and a transmembrane polypeptide *or* an Ig light chain and a transmembrane polypeptide. US Patent 6,015,884 claims the fusion protein, does not specifically claim a composition comprising a cell and fusion protein. However, Seimiya H *et al* does claim the combination of the cell and fusion protein.

Therefore, it would have been obvious to make a composition comprising a cell with the said fusion proteins because the 6,015,884 patent teaches the fusion constructs itself and Seimiya H *et al* also teaches the fusion construct which is expressed in myeloma cells. One of ordinary skill would have been motivated to combine the references because although not explicitly claimed in the US Patent, in order for the fusion constructs to be made and expressed in the US Patent, it must have been expressed, at one point, in a cellular expression system wherein the fusion proteins were either extracted or isolated. Seimiya *et al* does specifically state the fusion constructs are expressed on the surface of the cell. One of ordinary skill would have expected a reasonable amount of success in combining the references because the fusion protein described is not a naturally occurring protein so in order for the protein to be made, it must have been in a cell. And because the protein described in the patent and in Seimiya H *et al* are functional, one of skill could reasonable expect that leaving the protein intact on the surface of the cell would be a reasonable form of storage or functional use.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 28,30-32, 53 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuwana *et al* (Biochem Biophys Res Commun 1987 Dec;149(3):960-

968). Claims are drawn to a composition comprising a cell in which a molecular complex is attaches to the surface of the cell, wherein the molecular complex comprises at least four fusion proteins that are either an Ig variable heavy chain and an extracellular portion of a transmembrane polypeptide or an Ig variable light chain and an extracellular portion of a transmembrane polypeptide. The claims are further limited by the extracellular transmembrane polypeptide being TCR α and TCR β chains, the molecular complex being bound by antigenic peptides, the fusion proteins being linked by a linker sequence, and the antigenic peptide being bound by a method of incubating the cell with the said antigenic peptide.

Kuwana *et al* disclose an EL4 cell expressing a chimeric receptor on the surface of the said cell, comprising variable light chain linked to TCR β, variable heavy chain linked to TCR β, variable light chain linked to TCR α, and variable heavy chain linked to TCR β. Kuwanw *et al* further disclose the linking of the fusion protein by a linker (see page 963) and mixing/incubating EL4 cells with an antigenic peptide (see page 965 2nd paragraph).

Claim Rejections - 35 USC § 102

11. Claims 28, 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Seimiya H *et al*. Claims are drawn to a composition comprising a cell in which a molecular complex is attaches to the surface of the cell, wherein the molecular complex comprises at least four fusion proteins that are either an Ig variable heavy chain and an extracellular portion of a transmembrane polypeptide or an Ig variable light chain and an

extracellular portion of a transmembrane polypeptide. The claims are further limited by the extracellular transmembrane polypeptide being TCR α and TCR β chains.

Seimiya *et al* disclose SP2/0 myeloma cells expressing a TCR-α or β protein linked to Ig molecule. Although not explicitly disclosed, in the absence of evidence to the contrary, the expression construct making the fusion protein was transfected into the mammalian cell and therefore multiple copies of fusion protein would be present one the cell surface.

Claim Rejections - 35 USC § 102

12. Claims 28, 29, 31, 32, 51, 56, and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Zwirner J *et al* (J. Immunol. 1992 Jan;148(1):272-276). Claims are drawn to a composition comprising a cell in which a molecular complex is attaches to the surface of the cell, wherein the molecular complex comprises at least four fusion proteins that are either an Ig variable heavy chain and an extracellular portion of a transmembrane polypeptide or an Ig variable light chain and an extracellular portion of a transmembrane polypeptide. The claims are further limited by the extracellular transmembrane polypeptide being MHC class IIα and MHC class IIβ chains, an antigenic peptide being bound to the fusion proteins, the variable Ig heavy chain being of IgG1 subtype, the antigenic peptide being bound by mixing/incubating with the cell, and the molecular complex being conjugated to an effector molecule that is capable of eliciting an immune response.

Zwirner J *et al* disclose a mouse B-cell lymphoma cell line (A20) expressing a chimeric MHC class II-Ig fusion protein wherein the MHC class II are α or β chains and

the Ig is of the IgG1 subtype. It is also disclosed that the chimeric protein was expressed on the surface of the cell and that such expression resulted in a properly folded functional receptor capable of binding to an antigen or ligand. Zwirner J *et al* further teach that the chimeric protein bound to an anti-idiotypic antibody (assays were performed wherein the antibody was incubated with the A20 cell line see pages 274 and 275), and because the anti-idiotypic antibody contains an Fc region, it fulfills the limitation of an effector molecule that stimulates/eliciting an immune response.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 28-32, 51-53, 56, 58, and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuwana *et al*, Zwirner *et al*, and Selick *et al* (WO 93/10220). See above for limitations to claims 28-32, 51, 53, and 56. The claims are further limited to the variable light chain being a Igκ chain, and the antigenic peptide being bound covalently. See paragraphs 11 and 13, supra, for Kuwana *et al* and Zwirner *et al* disclosures. Kuwana *et al* and Zwirner *et al* do not specifically teach the use of an Ig κ chain or that an antigenic peptide be covalently bound to the fusion protein. However, Selick *et al* do teach using both an Ig κ chain and to covalently link the antigenic peptide to the fusion construct.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make and use a composition comprising a cell which expresses on its surface at least four fusion proteins wherein there is two variable Ig heavy chains that are of IgG1 subtype fused to a transmembrane polypeptide and two variable light chains that are of Ig κ subtype fused to a transmembrane polypeptide, wherein an antigenic protein is covalently linked to the binging domain of the fusion protein. One would have been motivated to combine the references because the references teach the utilization of a composition that comprises α and β subunits of MHC or TCR molecules fused with antibody fragments. Although both Kuwana *et al* and Zwirner *et al* do not specifically teach the construction of the fusion constructs with Ig κ subunits, it would have been obvious because there are essentially only two types of Ig light chains (the other being lambda) that could have been used in the construction. Further, Kuwana *et al* discusses assays wherein ligands to the chimeric protein can be used to test for proper function. One of skill would have found it obvious to covalently attach the ligand to the fusion protein because by doing so, a specific response could have been elicited to the specific antigen upon administration. One of skill would have expected a reasonable amount of success in making the composition because most of the limitations to the composition were already taught, wherein the functional characterization was performed and there would be little functional difference in substituting one type of light chain for another.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
June 16, 2003

ANTHONY C. CAPUTA
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